

In the Claims

Please amend page 56, line 1 as follows:

Claims (revised) What is claimed is:

This listing of claims will replace all prior versions, and listings, including the original set of claims Published and the amended sheets attached to the IPER of claims in the application. These amendments reflect the amended claims based on the IPER.

Listing of Claims:

1. (Original) An imaging agent which comprises a synthetic barbituric acid matrix metalloproteinase inhibitor labelled at the 5-position of the barbituric acid with an imaging moiety, wherein the imaging moiety can be detected following administration of said labelled synthetic barbituric acid matrix metalloproteinase inhibitor to the mammalian body *in vivo*, and said imaging moiety is chosen from:
 - (i) a radioactive metal ion;
 - (ii) a paramagnetic metal ion;
 - (iii) a gamma-emitting radioactive halogen;
 - (iv) a positron-emitting radioactive non-metal;
 - (v) a hyperpolarised NMR-active nucleus;
 - (vi) a reporter suitable for *in vivo* optical imaging;
 - (vii) a β -emitter suitable for intravascular detection.
2. (Original) The imaging agent of Claim 1, where the synthetic barbituric acid matrix metalloproteinase inhibitor ligand conjugate is of Formula I:



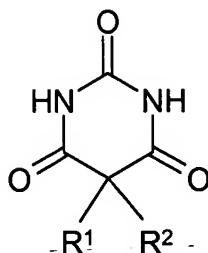
where:

{inhibitor} is the synthetic barbituric acid matrix metalloproteinase inhibitor;

$-(A)_n-$ is a linker group wherein each A is independently $-CR_2-$, $-CR=CR-$, $-C\equiv C-$, $-CR_2CO_2-$, $-CO_2CR_2-$, $-NRCO-$, $-CONR-$, $-NR(C=O)NR-$, $-NR(C=S)NR-$, $-SO_2NR-$, $-NRSO_2-$, $-CR_2OCR_2-$, $-CR_2SCR_2-$, $-CR_2NRCR_2-$, a C_{4-8} cycloheteroalkylene group, a C_{4-8} cycloalkylene group, a C_{5-12} arylene group, or a C_{3-12} heteroarylene group, an amino acid or a monodisperse polyethyleneglycol (PEG) building block;
R is independently chosen from H, C_{1-4} alkyl, C_{2-4} alkenyl, C_{2-4} alkynyl, C_{1-4} alkoxyalkyl or C_{1-4} hydroxyalkyl;
n is an integer of value 0 to 10; and
m is 1, 2 or 3.

3. (Currently amended) The imaging agent of ~~Claims 1 or 2~~ claim 1, where the synthetic barbituric acid matrix metalloproteinase inhibitor is conjugated to a ligand, and said ligand forms a metal complex with the radioactive metal ion or paramagnetic metal ion.
4. (Original) The imaging agent of Claim 3, where the ligand is a chelating agent.
5. (Currently amended) The imaging agent of ~~Claims 3 or 4~~ claim 3, where the radioactive metal ion is a gamma emitter or a positron emitter.
6. (Original) The imaging agent of Claim 5, where the radioactive metal ion is ^{99m}Tc , ^{111}In , ^{64}Cu , ^{67}Cu , ^{67}Ga or ^{68}Ga .
7. (Currently amended) The imaging agent of ~~Claims 1 or 2~~, claim 1 where the gamma-emitting radioactive halogen imaging moiety is ^{123}I .
8. (Currently amended) The imaging agent of ~~Claims 1 or 2~~ claim 1, where the positron-emitting radioactive non-metal is chosen from ^{18}F , ^{11}C or ^{13}N .

9. (Currently amended) The imaging agent of ~~Claims 1 to 8~~claim 1, where the synthetic



barbituric acid matrix metalloproteinase inhibitor is of Formula IV:

(IV)

where:

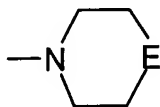
R¹ is R" or a Z group;

R² is R", Y or -NR⁴R⁵, where R⁴ is H or an R" group, R⁵ is H, C₂₋₁₄ acyl, C₂₋₁₀ aminoalkyl or (N-C₂₋₁₄ acyl)C₂₋₁₀ aminoalkyl or an R" group, or R⁴ and R⁵ together with the N atom to which they are attached form an optionally (N-C₂₋₁₄)acylated C₂₋₈ cycloaminoalkylene ring;

R" is independently C₁₋₁₄ alkyl, C₃₋₈ cycloalkyl, C₂₋₁₄ alkenyl, C₁₋₁₄ fluoroalkyl, C₁₋₁₄ perfluoroalkyl, C₆₋₁₄ aryl, C₂₋₁₄ heteroaryl or C₇₋₁₆ alkylaryl;

Z is a group of formula -A¹O[A²O]_pR³ where p is 0 or 1, and A¹ and A² are independently C₁₋₁₀ alkylene, C₃₋₈ cycloalkylene, C₁₋₁₀ perfluoroalkylene, C₆₋₁₀ arylene or C₂₋₁₀ heteroarylene, and R³ is an R group where R is independently chosen from H, C₁₋₄ alkyl, C₂₋₄ alkenyl, C₂₋₄ alkynyl, C₁₋₄ alkoxyalkyl or C₁₋₄ hydroxyalkyl;

Y is a group of formula:

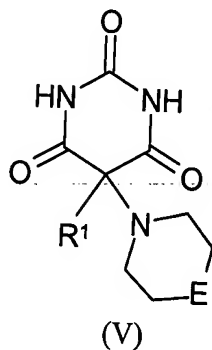


where E is CR₂, O, S or NR⁶; and R⁶ is C₂₋₁₄ acyl, or an R" or Z group.

10. (Original) The imaging agent of claim 9, where R² is Y or -NR⁴R⁵.

11. (Currently amended) The imaging agent of ~~claims 9 or 10~~ claim 9, where the imaging moiety is attached to the R² substituent.

12. (Currently amended) The imaging agent of ~~claims 9 to 11~~ claim 9, of Formula V:



where E is CHR or NR⁶ and R¹ is C₆₋₁₄ *n*-alkyl, or C₆₋₁₄ aryl.

13. (Original) The imaging agent of claim 12, where E is NR⁶ and R⁶ is C₂₋₁₄ acyl; – (CH₂)_dOH, where d is 2, 3, 4 or 5; or –C₆H₄X, where X is H, C₁₋₄ alkyl, Hal, OR, NR₂, NO₂ or SO₂NR⁷R⁸, where R⁷ and R⁸ are independently R groups, and R is as defined in Claim 9.

14. (Currently amended) The imaging agent of ~~claims 12 or 13~~ claim 12, where R¹ is *n*-octyl, *n*-decyl, biphenyl, C₆H₅X or –C₆H₄–O–C₆H₄X where X is as defined in Claim 13.

15. (Currently amended) A pharmaceutical composition which comprises the imaging agent of ~~claims 1 to 14~~ claim 1 together with a biocompatible carrier, in a form suitable for mammalian administration.

16. (Currently amended) A radiopharmaceutical composition which comprises the imaging agent of ~~claims 1 to 14~~ claim 1, wherein the imaging moiety is radioactive, together with a biocompatible carrier, in a form suitable for mammalian administration.

17. (Original) The radiopharmaceutical composition of claim 16, where the imaging moiety comprises a radioactive metal ion.
18. (Original) The radiopharmaceutical composition of claim 16, where the imaging moiety comprises a positron-emitting radioactive non-metal or a gamma-emitting radioactive halogen.
19. (Original) A conjugate of a synthetic barbituric acid matrix metalloproteinase inhibitor with a ligand, wherein the barbituric acid comprises a 5-position substituent, and said 5-position substituent comprises a ligand capable of forming a metal complex with a radioactive or paramagnetic metal ion which is resistant to transchelation.
20. (Original) The conjugate of Claim 19, of Formula Ib:
- $$[\{\text{inhibitor}\}-(A)_n]_m-[\text{ligand}] \quad (\text{Ib}),$$
- where {inhibitor}, A, n and m are as defined in Claim 2.
21. (Currently amended) The conjugate of ~~Claims 19 or 20~~claim 19, wherein the synthetic barbituric acid matrix metalloproteinase inhibitor is of Formula IV or Formula V of Claims 9 to 14.
22. (Currently amended) The conjugate of ~~Claims 19 to 21~~claim 19, wherein the ligand is a chelating agent.
23. (Original) The conjugate of Claim 22, wherein the chelating agent has a diaminedioxime, N_2S_2 , or N_3S donor set.
24. (Currently amended) A kit for the preparation of the radiopharmaceutical composition of Claim 17, which comprises ~~the conjugates of Claims 19 to 23:~~
a conjugate of a synthetic barbituric acid matrix metalloproteinase inhibitor with a ligand, wherein the barbituric acid comprises a 5-position substituent, and said 5-

position substituent comprises a ligand capable of forming a metal complex with a radioactive or paramagnetic metal ion which is resistant to transchelation, said conjugate being of Formula Ib:



where {inhibitor}, A, n and m are as defined in Claim 2; and

wherein the ligand is a chelating agent.

25. (Original) The kit of Claim 26, where the radioactive metal ion is ^{99m}Tc , and the kit further comprises a biocompatible reductant.
26. (Currently amended) A kit for the preparation of the radiopharmaceutical composition of Claim 18, which comprises a precursor in sterile form which is a non-radioactive derivative of the barbituric acid matrix metalloproteinase inhibitor of claims 1-~~14~~14, wherein said non-radioactive derivative is capable of reaction with a source of the positron-emitting radioactive non-metal or gamma-emitting radioactive halogen to give the desired radiopharmaceutical.
27. (Original) The kit of Claim 26, where the source of the positron-emitting radioactive non-metal or gamma-emitting radioactive halogen is chosen from:
- (i) halide ion;
 - (ii) F^+ or I^+ ; or
 - (iii) an alkylating agent chosen from an alkyl or fluoroalkyl halide, tosylate, triflate or mesylate;
 - (iv) $\text{HS}(\text{CH}_2)_3^{18}\text{F}$.
28. (Currently amended) The kit of ~~claims 26 or 27~~ claim 26, wherein the non-radioactive derivative is chosen from:
- (i) an organometallic derivative such as a trialkylstannane or a trialkylsilane;
 - (ii) a derivative containing an alkyl or aryl iodide or bromide, alkyl tosylate or alkyl mesylate for nucleophilic substitution;

- (iii) a derivative containing an aromatic ring activated towards nucleophilic or electrophilic substitution;
- (iv) a derivative containing a functional group which undergoes facile alkylation;
- (v) a derivative which undergoes alkylation with an alkyl thiol to give a thioether.

29. (Currently amended) The kit of ~~claims 26 to 28~~claim 26, where the precursor is bound to a solid phase.
30. (Currently amended) Use of the imaging agent of ~~Claims 1 to 14~~ claim 1 for the diagnostic imaging of atherosclerosis.
31. (Currently amended) Use of the imaging agent of ~~Claims 1 to 14~~ claim 1 for the diagnostic imaging of unstable plaques.
32. (Currently amended) Use of the imaging agent of ~~Claims 1 to 14~~ claim 1 for the intravascular detection of atherosclerosis.